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Effectively detecting anomalous diffusion via deep learning

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A deep learning algorithm is presented to classify single-particle tracking trajectories into theoretical models of anomalous diffusion and detect if the trajectory is related to a model not originally found within the training dataset.

The diffusion of particles in different environments has been studied in the physical and biological sciences for more than a century. Originally, Einstein proposed a mathematical model to describe the observed erratic movement of particles suspended in a fluid, a random walk known as Brownian motion[1]. Einstein's model of Brownian motion has two landmarks seen in simple systems, such as the diffusion of small particles in water: the probability distribution of the particle displacements is Gaussian, and the mean of the squared displacements scales linearly with time[2]. During the last 20 years, the emergence of single-molecule techniques and single-particle tracking has provided important insights into the behavior of molecules and organelles within complex environments[3]. These new insights uncovered deviations from Brownian motion across a wide range of biophysical data. These observations show anomalous diffusion where the mean squared displacement does not scale linearly in time and the distribution of displacements may not be Gaussian. Several mathematical models have been proposed to describe the different features that give rise to anomalous diffusion[2,4,5]. However, effective models to characterize anomalous diffusions with unknown features are still lacking in the community. In this issue of *Nature Computational Science*, Xiaochen Feng and colleagues report a deep-learning approach that not only improves the precision in classifying trajectories into the anomalous diffusion models used in the training steps but also considers the possibility that such a trajectory belongs to a completely different type of motion[6] (Fig. 1).

With recent developments in machine learning (ML) algorithms and their successful application to many areas of science, it is no surprise that ML approaches were soon applied to the characterization of anomalous diffusion[7–9]. A recent objective study comparing different methods reveals that ML algorithms perform better at classifying anomalous diffusion trajectories than conventional statistical methods[9]. However, recent applications of ML methods to study anomalous diffusion mainly focus on classifying a given trajectory into various mathematical models and quantifying the deviations from normal diffusion. In fact, even when these ML classifiers can exhibit an improved performance in characterization, they face a fundamental challenge: if a trajectory lacks the features of the training models, such as the scaling of the mean squared displacement or the power spectral density[10], these approaches will lead to an incorrect classification.

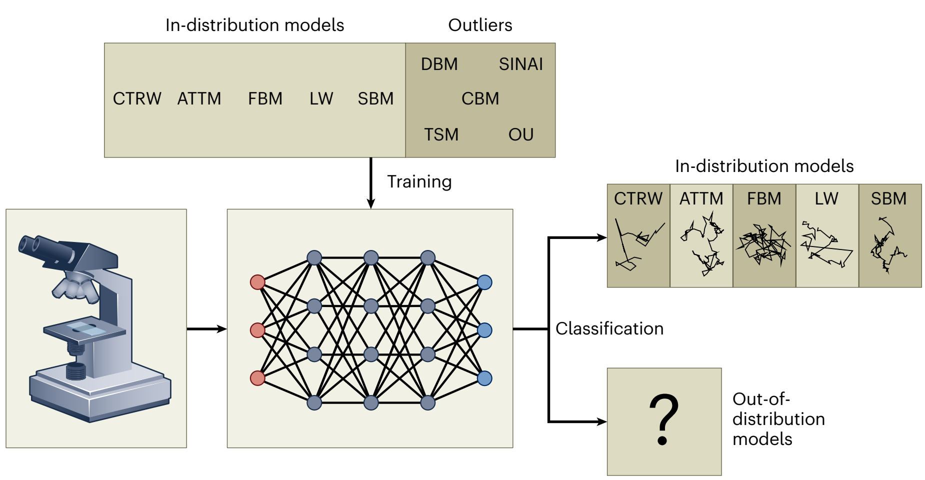

Fig. 1 | Workflow of the deep-learning approach for detecting anomalous diffusion. The deep-learning network is trained with trajectories of five anomalous diffusion models, the in-distribution model set. These models are continuous-time random walk (CTRW), annealed transient time model (ATTM), fractional Brownian motion (FBM), Lévy walks (LW), and scaled Brownian motion (SBM). Outlier trajectories are added to the training set belonging to five additional diffusion models, namely, directed Brownian motion (DBM), two-state model (TSM), combined anomalous diffusion motion (CBM), Sinai diffusion (SINAI), and Ornstein–Uhlenbeck (OU). Thus, when applying the deep-learning network to experimentally obtained trajectories, they are classified in one of the five in-distribution models. Yet, if any of these trajectories present features that do not correspond to any of them, it is classified as belonging to an out-of-distribution model. Thus, the classification is not constrained to the models used in the training step.

In other words, such a trajectory may present unknown features, and thus a different model should be considered.

In common deep-learning classification methods, the algorithm learns features of the training data and then tries to classify the test data among the different categories (models). In other words, one starts with the closed-world assumption that the test dataset also belongs to the models used in the training set, the so-called in-distribution models. Yet, this assumption is not always correct in real-world situations, highlighting the need for a more reliable classification method. To tackle this problem, Feng et. al. proposed an out-of-distribution classification method, which consists of a deep-learning network that accurately classifies trajectories belonging to the in-distribution anomalous diffusion models while at the same time being capable of identifying out-of-distribution trajectories. Following the Anomalous Diffusion (AnDi) challenge[9], a competition aimed at evaluating methods for detecting anomalous diffusion from individual trajectories, the authors select five models to create the in-distribution sample, namely continuous-time random walk, annealed transient time model, fractional Brownian motion, Lévy walk, and scaled Brownian motion. Using a Mixup procedure, the authors generate sample outliers that do not belong to the in-distribution models, but to five additional diffusion models, namely, directed Brownian motion, two-state model, combined anomalous diffusion motion, Sinai diffusion, and Ornstein–Uhlenbeck, as shown in Fig. 1. The analysis shows that trajectories identified as out-of-distribution are better described with these modes rather than with the ones used during training. With such an additional layer of complexity produced by the addition of these outliers, Feng and collaborators were able to improve the classification concerning the in-distribution models but also allowed good out-of-distribution classification.

In general, the limited number of models used in supervised machine learning poses one of the main setbacks in implementing these classifiers. The presented algorithm can be used to more reliably detect anomalous diffusion models, which in turn can lead to a better understanding of cellular processes and biomolecular interactions in the crowded realm inside living cells. While this work paves the way for strengthening our understanding of anomalous diffusion, it remains to be seen if using deep learning for out-of-distribution detection promotes the development of new theories to better model complex systems. In practice, the impact of this work depends on how easily researchers in different fields can implement these algorithms. The accurate identification of out-of-distribution models, as demonstrated in this work, not only enhances our understanding of anomalous diffusion but also holds potential for applications in other fields where reliable classification is crucial.

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Competing interests

The authors declare no competing interests.